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# Improved Drug Adherence Improves Cardiac Outcomes after Myocardial Infarction in Diabetic Patients

*Background* Diabetic patients face a higher risk of adverse cardiac events following myocardial infarction (MI). Medication adherence plays a key role in secondary prevention, but its specific impact on the prognosis of diabetic patients with MI has not been comprehensively evaluated.

*Material and methods* This retrospective cohort study analyzed medical records of 428 diabetic patients with acute MI over a 24-mo review period. Patient adherence to antiplatelet drugs, statins, β-blockers, and angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (ACEI/ARBs) was retrospectively assessed through medical records and patient interviews, categorized using the 8-item Morisky Medication Adherence Scale (MMAS-8). Primary endpoints included all-cause mortality, cardiovascular mortality, recurrent MI, and unplanned rehospitalization. Clinical indicators, including left ventricular ejection fraction (LVEF), N-terminal pro-brain natriuretic peptide (NT-proBNP), glycated hemoglobin (HbA1c), low-density lipoprotein cholesterol (LDL–C), blood pressure, and creatinine clearance rate (CrCl), were extracted and analyzed from electronic medical records. Cox proportional hazards models were used to analyze the association between medication adherence and clinical outcomes.

*Results* Retrospective analysis showed that, compared to patients with low adherence, patients with high adherence (MMAS-8 score ≥6) had a 42% reduction in all-cause mortality, a 38% reduction in cardiovascular mortality, and a 35% reduction in the risk of recurrent MI. Multivariate analysis showed that medication adherence was an independent predictor of adverse cardiovascular events. For clinical indicators, the high-adherence group performed significantly better in LVEF, NT-proBNP concentration, HbA1c control, LDL–C target achievement, blood pressure control, and CrCl stability.

*Conclusion* Retrospective data analysis indicates that medication adherence is significantly associated with cardiac outcomes in diabetic patients after MI. Improving medication adherence should reduce the occurrence of adverse cardiovascular events and improve key clinical indicators.

*Keywords* Medication adherence; diabetes mellitus; myocardial infarction; cardiovascular outcomes

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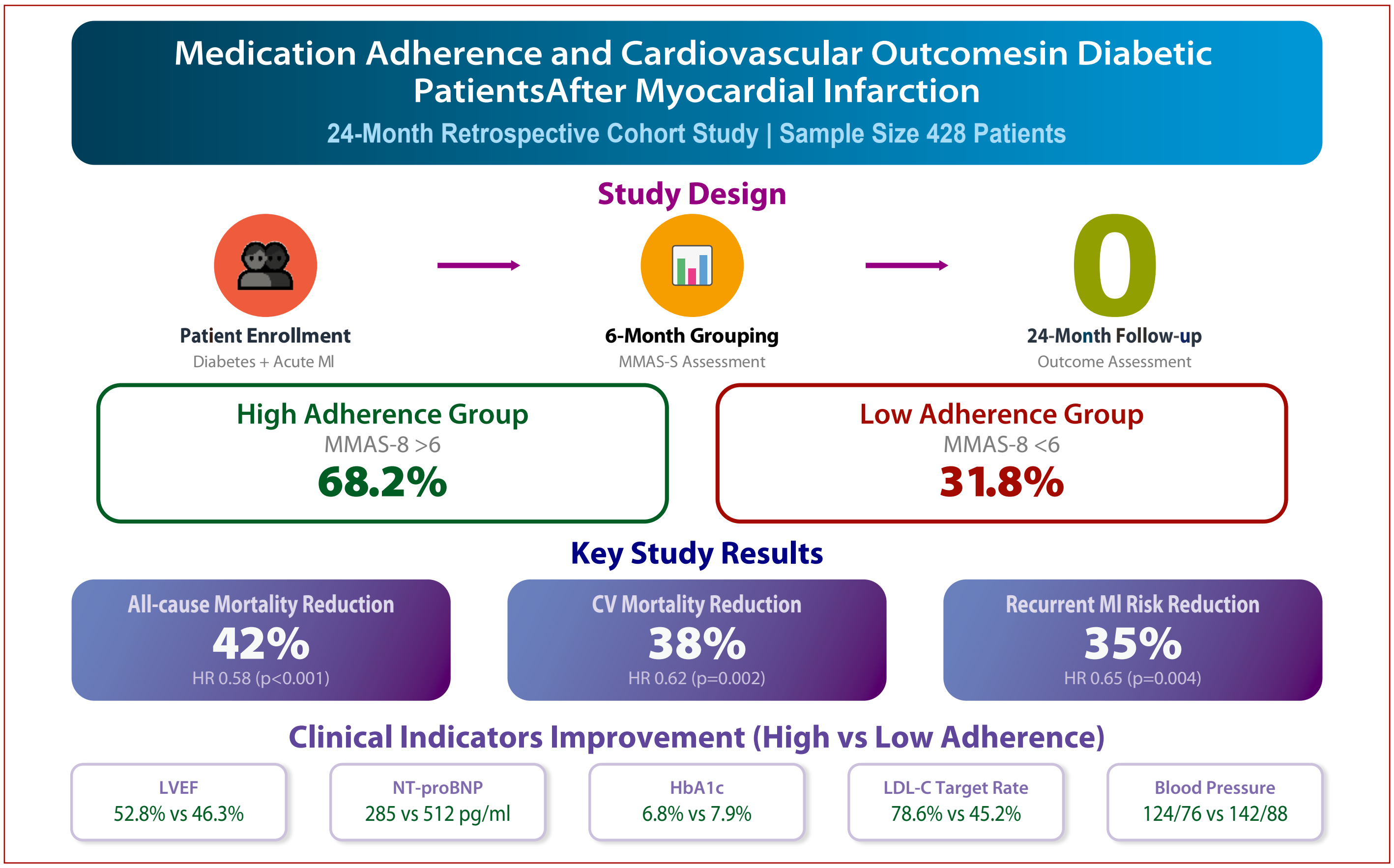
## Introduction

Myocardial infarction (MI) represents a significant health challenge worldwide, with particularly adverse implications for patients with diabetes mellitus. The intersection of these two conditions creates a complex clinical scenario characterized by elevated risks of recurrent cardiovascular events, including MI, stroke, heart failure, and mortality. Diabetic patients who experience MI face approximately twice the risk of adverse outcomes compared to non-diabetic counterparts, creating an urgent need for effective secondary prevention strategies [1, 2].

Secondary prevention medications, including antiplatelet agents, statins, beta-blockers, and angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (ACEI/ARBs), have demonstrated substantial benefits in reducing cardiovascular morbidity and mortality following MI [3, 4]. However, the efficacy of these evidence-based therapies is fundamentally dependent on patient compliance to prescribed medication regimens. Unfortunately, medication non-adherence remains a pervasive challenge in cardiovascular care, with studies suggesting that up to 50% of patients exhibit suboptimal adherence within the first year after MI [5, 6].

For diabetic patients post-MI, the consequences of medication non-adherence may be particularly severe due to their baseline elevated cardiovascular risk profile and complex pathophysiology, which involves accelerated atherosclerosis, endothelial dysfunction, prothrombotic states, and autonomic dysfunction [7, 8]. Despite the critical importance of medication adherence in this high-risk population, there is a paucity of comprehensive research specifically examining the relationship between adherence patterns and cardiac outcomes in diabetic patients following MI.

Central illustration. Improved Drug Adherence Improves Cardiac Outcomes after Myocardial Infarction in Diabetic Patients




MI: Myocardial Infarction; MMAS-S: 8-Item Morisky Medication Adherence Scale; HR: Hazards Ratio; CV: Cardiovascular; LVEF: Left Ventricular Ejection Fraction; NT-proBNP: N-Terminal pro-brain natriuretic peptide; LDL-C: Low-Density Lipoprotein Cholesterol.

The convergence of diabetes and MI represents a "perfect storm" in cardiovascular pathophysiology, with each condition exacerbating the progression of the other [9]. Diabetes-induced metabolic abnormalities, including hyperglycemia, insulin resistance, and dyslipidemia, accelerate post-infarction adverse myocardial remodeling and impair cardiac repair mechanisms. These pathological processes can be significantly mitigated by consistent adherence to evidence-based medications [10, 11]. Studies have demonstrated that antiplatelet therapy reduces platelet hyperreactivity common in diabetic patients [12], while statins not only lower cholesterol but also stabilize atherosclerotic plaques and reduce inflammation [13]. Beta-blockers improve myocardial energetics and reduce sympathetic overactivation, while ACEI/ARBs counteract the deleterious effects of the renin-angiotensin-aldosterone system on cardiac remodeling [14].

Medication adherence in diabetic patients after MI can be conceptualized as a critical mediator between prescribed therapy and clinical outcomes. Several international registries have documented alarming gaps between guideline-recommended therapy and real-world medication persistence [6, 15, 16]. A particularly concerning pattern is the progressive decline in adherence over time, with many patients discontinuing essential cardioprotective medications within 6–12 mos after hospitalization [17]. This decline occurs precisely when the benefits of these medications in preventing adverse cardiac remodeling, recurrent ischemic events, and heart failure are most crucial.

The determinants of medication adherence in this patient population are multifactorial. They include socioeconomic factors (cost, access to healthcare), patient-related factors (health literacy, beliefs about medications, competing health priorities), medication-related factors (complexity of regimen, side effects), and healthcare system factors (continuity of care, quality of discharge education) [18–20]. Understanding these determinants is essential for designing effective interventions to enhance adherence [21].

Furthermore, traditional care models often fail to address the multifaceted barriers to medication adherence faced by diabetic patients after MI [22]. These barriers may include limited health literacy, medication complexity, concerns about side effects, financial constraints, and psychological factors such as post-MI depression or diabetes distress. Nursing interventions targeting these barriers represent a promising yet underutilized approach to improving adherence and, consequently, clinical outcomes [23].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The integration of objective clinical indicators, such as left ventricular ejection fraction (LVEF), N-terminal pro-brain natriuretic peptide (NT-proBNP), glycated hemoglobin (HbA1c), and lipid profiles, provides valuable metrics for assessing the physiological impact of medication adherence. These parameters can serve as both outcome measures and motivational feedback for patients, potentially reinforcing adherence behaviors through demonstrated clinical improvements.

This study aimed to address significant gaps in the current literature by:

1. Quantifying the association between medication adherence and comprehensive cardiovascular outcomes in diabetic patients following MI.
2. Identifying specific clinical indicators that reflect the physiological benefits of adherence.
3. Evaluating the effectiveness of structured nursing interventions in improving medication adherence and self-management capabilities in this high-risk population.

The results may in the development of targeted, evidence-based interventions to enhance medication adherence and improve long-term prognosis for diabetic patients after MI.

## Material and methods

### *Study design and patient population*

This retrospective cohort study analyzed data from Yan'an People's Hospital between January 2021 and January 2023. We initially enrolled consecutive patients diagnosed with acute MI (both ST-elevation myocardial infarction [STEMI] and non-ST-elevation myocardial infarction [NSTEMI]) who had a confirmed diagnosis of type 2 diabetes mellitus. The study was designed to investigate the association between medication adherence and cardiac outcomes in this high-risk population, with particular attention to the impact of nursing interventions on improving adherence. The study protocol was approved by the Institutional Ethics Committee (approval number IEC-2020-CVD-375), and written informed consent was obtained from all participants prior to enrollment.

The decision to focus specifically on diabetic patients with MI was based on several considerations. First, this population represents a particularly high-risk group with complex medication regimens and elevated rates of recurrent cardiovascular events. Second, preliminary research suggested that adherence patterns in diabetic patients may differ from those of the general post-MI population due to the additional burden of diabetes management. Finally, there was a notable gap in the literature regarding targeted interventions for this specific patient population, despite their disproportionate representation in cardiovascular morbidity and mortality statistics.

### *Inclusion and exclusion criteria*

Patients were eligible for *inclusion* if they met the following *criteria*:

1) Age ≥18 yrs;
2) Confirmed diagnosis of acute MI according to the Fourth Universal Definition of Myocardial Infarction as indicated by elevated cardiac troponin with at least one value above the 99$^{th}$ percentile upper reference limit accompanied by at least one of the following symptoms of myocardial ischemia:

- new ischemic electrocardiogram [ECG] changes with development of pathological Q waves;
- imaging evidence of new loss of viable myocardium;
- established diagnosis of type 2 diabetes mellitus (prior diagnosis or HbA1c ≥6.5% at admission);
- prescribed at least two classes of guideline-recommended post-MI medications (antiplatelet agents, statins, beta-blockers, ACEI/ARBs);
- Ability to provide informed consent and complete follow-up assessments.

*Exclusion criteria* were designed to minimize confounding factors and ensure reliable follow-up data. We excluded patients with:

1) Severe cognitive impairment affecting ability to self-administer medications or participate in follow-up assessments;
2) Life expectancy <24 mos due to non-cardiac comorbidities such as advanced malignancy or end-stage renal disease;
3) Planned surgery requiring discontinuation of dual antiplatelet therapy (DAPT) within 12 mos of enrollment;
4) Known contraindications to multiple classes of guideline-recommended medications that would necessitate non-standard treatment approaches;
5) Concurrent participation in another interventional clinical trial that could influence medication adherence or outcomes;
6) Pregnancy or planned pregnancy during the study period (due to potential medication contraindications);
7) Severe psychiatric disorders that would impair adherence with the study protocol, including active substance abuse or psychotic disorders.

Of the 503 patients initially screened, 428 met the inclusion criteria and consented to participate. The most common reasons for exclusion were severe comorbidities that limited life expectancy (n=28), cognitive impairment (n=19), and unwillingness to participate in follow-up assessments (n=15).

### *Patient grouping and follow-up schedule*

All enrolled patients received standardized inpatient cardiac rehabilitation and medication education before discharge. Initial assessment of medication adherence was performed at hospital discharge using the 8-item Morisky Medication Adherence Scale (MMAS-8) [24]. This baseline measurement served as a reference point for subsequent evaluations, but it was not used for group stratification due to the controlled hospital environment.

At the 6-month follow-up assessment, the patients were stratified into two groups based on their MMAS-8 scores: high adherence group (MMAS-8 score ≥6) and low adherence group (MMAS-8 score <6). This time point was selected for stratification based on previous research indicating that adherence patterns tend to stabilize within 3–6 mos after discharge, and that these patterns are predictive of long-term adherence behavior. The 6-mos timeframe also allowed sufficient opportunity for patients to establish medication routines outside the heightened vigilance period immediately following hospitalization.

Follow-up visits were scheduled at 6, 12, and 24 mos after the index MI event. Additional, unscheduled visits were documented if patients presented with recurrent cardiovascular symptoms or events. To minimize patient loss during follow-up, multiple contact methods were employed, including telephone reminders, text message alerts, and coordination with primary care providers. Patients who missed scheduled visits received up to three telephone contact attempts and, if unsuccessful, a home visit was arranged when feasible. Patients were considered lost to follow-up and removed from the study if: (1) they could not be reached after three telephone contact attempts on different days and times, followed by an unsuccessful home visit attempt; (2) they explicitly withdrew consent for continued participation; (3) they relocated outside the study catchment area without providing new contact information; or (4) death was confirmed through medical records or family notification. Patients who missed a single scheduled visit but were successfully contacted and remained willing to participate were retained in the study. A total of 15 patients were lost to follow-up for various reasons: 12 could not be contacted despite multiple attempts, 1 withdrew consent, and 2 relocated outside the study area.

### *Medication adherence assessment*

Medication adherence was comprehensively assessed using both subjective and objective measures to enhance reliability. The primary tool was the 8-item MMAS-8, administered at baseline, 6, 12 and 24 mos after the index MI event. This scale evaluates adherence through questions regarding forgetfulness (e.g., "Do you sometimes forget to take your medications?"), deliberate discontinuation (e.g., "When you feel better, do you sometimes stop taking your medications?"), and consistency of medication-taking behavior (e.g., "Did you take all your medications yesterday?"). Total scores ranged from 0 to 8, with higher scores indicating better adherence. Based on established validation studies, scores ≥6 were classified as high adherence, while scores <6 were classified as low adherence [24–26].

To complement self-reported adherence data, pharmacy refill records were obtained with patient consent. These records provided an objective measure of medication adherence, calculated as the proportion of days covered (PDC) for each medication class. PDC was defined as the ratio of the number of days covered by dispensed medication to the total number of days in the observation period, multiplied by 100%. A PDC ≥80% was considered indicative of good adherence based on consensus standards in pharmacoepidemiologic research [27, 28].

Additionally, pill counts were performed during follow-up visits to provide a third adherence measurement dimension. Patients were instructed to bring all their medication containers to each visit, where the number of remaining doses was counted and compared with the expected number based on prescription dates and dosing instructions. Concordance between these multiple adherence measures was analyzed to identify potential discrepancies between self-reported and objective adherence indicators.

### *Nursing intervention protocol*

All patients received standard discharge education before leaving the hospital, which included basic medication information, lifestyle recommendations, and follow-up instructions. After the 6-mo assessment and subsequent group stratification, participants in the low adherence group received additional structured nursing interventions specifically designed to address common barriers to medication adherence.

The enhanced nursing intervention program was multifaceted and individualized, consisting of several components:

1) Personalized medication education sessions conducted by cardiovascular nurse specialists, focusing on the mechanisms of action, expected benefits, potential side effects, and proper administration of each prescribed medication;
2) Collaborative medication regimen simplification where clinically appropriate and in consultation with the patient's cardiologist and endocrinologist. This simplification included consolidation of dosing schedules, use of combination pills where available, and alignment of administration times with daily routines.
3) Provision of practical medication management tools such as pill organizers, medication calendars, and smartphone reminder applications based on patient preference and technological literacy;
4) Structured monthly telephone follow-up for problem-solving, addressing emerging concerns, and providing positive reinforcement for adherence behaviors;
5) Engagement of family members or caregivers in medication management processes with patient consent, inclu-


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ding education on the importance of adherence and strategies for providing supportive assistance without compromising patient autonomy.

The nurses that delivered the enhanced intervention program had completed standardized training in motivational interviewing techniques and were certified in diabetes self-management education. Intervention fidelity was monitored through random auditing of session recordings and regular supervisory meetings. The intensity and focus of interventions were tailored, based on identified barriers to adherence, with more intensive support provided to patients with multiple barriers or particularly complex medication regimens.

### *Clinical and laboratory assessments*

A comprehensive set of clinical and laboratory parameters was assessed at baseline and at 6, 12, and 24 mos to evaluate both the direct effects of medication adherence on pathophysiological markers and the on the ultimate impact of clinical outcomes. To minimize potential bias, these assessments were performed by clinicians blinded to patients' adherence group classification.

Clinical indicators were selected based on their established relevance to cardiovascular prognosis in diabetic patients with MI and on their potential responsiveness to evidence-based pharmacotherapy. LVEF was measured by transthoracic echocardiography using the modified Simpson's biplane method, with all studies performed according to standardized protocols and interpreted by experienced echocardiographers. Blood samples for biochemical parameter assays were collected from participants in a fasted state. N-terminal pro-brain natriuretic peptide (NT-proBNP) was analyzed using an electrochemiluminescence immunoassay. Glycated hemoglobin (HbA1c) was measured using high-performance liquid chromatography in a nationally certified laboratory. For low-density lipoprotein cholesterol (LDL–C) determination, total cholesterol, high-density lipoprotein cholesterol (HDL–C), and triglycerides were measured using enzymatic methods on an automated analyzer. When triglycerides were <400 mg/dl, LDL–C was calculated using the Friedewald formula:

$$\text{LDL–C} = \text{Total cholesterol} - \text{HDL–C} - (\text{Triglycerides}/5).$$

For samples with triglycerides ≥400 mg/dl, LDL–C was directly measured using a homogeneous enzymatic assay. Blood pressure measurements were obtained using calibrated automated devices after at least 5 min rest, and the average of three consecutive readings was recorded. Creatinine clearance rate (CrCl) was calculated using the Cockcroft-Gault formula adjusted for body surface area.

In addition to these physiological and biochemical parameters, we assessed two key nursing indicators reflecting patients' capacity for effective medication self-management. Medication knowledge was evaluated using a 10-point questionnaire developed for this study. The questionnaire items were adapted from the Medication Understanding and Use Self-Efficacy Scale (MUSE) [29]. It covers the name, purpose, dosage, timing, and potential side effects of each prescribed medication. The questionnaire underwent pilot testing with 25 participants similar to our target population, demonstrating good internal consistency (Cronbach's $\alpha$=0.89). Content validity was established through expert review by seven healthcare professionals (three pharmacists, two physicians, and two nurse specialists) with expertise in medication management for chronic conditions. Self-management ability was assessed using a 10-point scale developed for this study. The scale evaluated confidence and skills in medication management, symptom monitoring, and implementation of lifestyle modifications. Items and dimensions were adapted from the Chronic Disease Self-Efficacy Scale [30]. The scale underwent pilot testing with 30 participants, demonstrating good internal consistency (Cronbach's $\alpha$ = 0.87) and content validity through expert review by five healthcare professionals specializing in chronic disease management.

### *Study endpoints*

The study endpoints were designed to capture both clinical outcomes and intermediate markers of treatment effectiveness. Primary endpoints included:

1. All-cause mortality, cardiovascular mortality (defined as death due to MI, heart failure, sudden cardiac death, or other documented cardiovascular causes).
2. Recurrent MI (defined according to the Fourth Universal Definition of Myocardial Infarction).
3. Unplanned rehospitalization for cardiovascular causes (including acute coronary syndrome, heart failure, arrhythmia, or stroke). All endpoint events were adjudicated by an independent clinical events committee blinded to patients' adherence status, using standardized definitions and requiring supporting documentation from hospital records.

Secondary endpoints encompassed:

1. Changes in medication adherence scores over the 24-mo follow-up period.
2. Changes in medication knowledge and self-management ability scores.
3. Changes in six clinical indicators (LVEF, NT-proBNP, HbA1c, LDL–C, blood pressure, and CrCl).
4. A composite of major adverse cardiovascular events (MACE), defined as the combination of cardiovascular death, recurrent MI, and stroke. This composite endpoint is widely used in cardiovascular research and provides a comprehensive assessment of serious adverse outcomes.

**Table 1.** Baseline characteristics of high and low adherence patients

| Characteristic | High Adherence Group (n=237) | Low Adherence Group (n=191) | p-value |
|---|---|---|---|
| **Demographic Characteristics** | | | |
| Age (yrs), Mean±SD | 62.4±8.5 | 64.2±9.1 | 0.12 |
| Male, n (%) | 144 (60.5) | 124 (65.2) | 0.34 |
| BMI (kg/m²), Mean±SD | 27.5±3.2 | 28.1±3.5 | 0.21 |
| Education level (college and above), n (%) | 107 (45.1) | 54 (28.3) | 0.01 |
| **MI Type** | | | |
| STEMI, n (%) | 125 (52.7) | 101 (52.9) | 0.97 |
| NSTEMI, n (%) | 112 (47.3) | 90 (47.1) | |
| **Medical History** | | | |
| Duration of diabetes (yrs), Mean±SD, n (%) | 8.3±5.7 | 8.9±6.1 | 0.19 |
| Prior MI, n (%) | 44 (18.6) | 39 (20.4) | 0.58 |
| Hypertension, n (%) | 203 (85.6) | 167 (87.4) | 0.52 |
| Hypercholesterolemia, n (%) | 107 (45.1) | 92 (48.2) | 0.40 |
| Smoking history, n (%) | 71 (30.0) | 61 (35.1) | 0.23 |
| Alcohol consumption, n (%) | 36 (15.2) | 35 (18.3) | 0.34 |
| Family history of diabetes, n (%) | 85 (35.8) | 64 (33.5) | 0.57 |
| Comorbidity count, Mean±SD | 3.2±1.3 | 3.8±1.5 | 0.03 |
| **Treatment Modalities** | | | |
| Percutaneous coronary intervention, n (%) | 187 (78.9) | 145 (75.9) | 0.31 |
| Coronary artery bypass grafting, n (%) | 15 (6.3) | 16 (8.4) | 0.39 |
| Medical therapy, n (%) | 35 (14.8) | 30 (15.7) | 0.78 |
| **Medication Therapy** | | | |
| Antiplatelet agents, n (%) | 234 (98.7) | 189 (99.0) | 0.82 |
| DAPT, n (%) | 212 (89.5) | 171 (89.5) | 0.99 |
| Statins, n (%) | 229 (96.6) | 185 (96.9) | 0.85 |
| β-blockers, n (%) | 224 (94.5) | 180 (94.2) | 0.89 |
| ACEI/ARB, n (%) | 218 (92.0) | 175 (91.6) | 0.89 |
| Total cardiovascular medications, Mean±SD | 4.9±1.0 | 5.8±1.2 | <0.01 |
| **Baseline Clinical Indicators** | | | |
| LVEF (%), Mean±SD | 45.2±6.7 | 44.8±7.1 | 0.38 |
| NT-proBNP (pg/ml), Mean±SD | 628±253 | 645±267 | 0.28 |
| HbA1c (%), Mean±SD | 7.8±1.4 | 7.9±1.5 | 0.42 |
| LDL–C (mmol/l), Mean±SD | 3.2±0.8 | 3.3±0.7 | 0.36 |
| HDL–C (mmol/l), Mean±SD | 1.2±0.3 | 1.1±0.2 | 0.18 |
| Triglycerides (mmol/l), Mean±SD | 1.8±0.6 | 2.0±0.8 | 0.14 |
| Systolic blood pressure (mmHg), Mean±SD | 138±16 | 141±15 | 0.17 |
| Diastolic blood pressure (mmHg), Mean±SD | 85±9 | 87±8 | 0.17 |
| CrCl (ml/min), Mean±SD | 76.8±18.2 | 74.5±19.4 | 0.22 |
| Fasting plasma glucose (mmol/l), Mean±SD | 7.1±1.5 | 7.4±1.7 | 0.31 |
| **Adherence-Related Indicators** | | | |
| MMAS-8 score, Mean±SD | 7.2±1.1 | 4.5±1.0 | <0.001 |
| Medication knowledge score, Mean±SD | 7.8±1.2 | 5.3±1.8 | <0.001 |
| Self-management ability score, Mean±SD | 8.2±1.5 | 6.1±1.9 | <0.001 |

SD: Standard Deviation; BMI: Body Mass Index; STEMI: ST-segment Elevation Myocardial Infarction; NSTEMI: Non-ST Segment Elevation Myocardial Infarction; MI: Myocardial Infarction; DAPT: Dual Antiplatelet Therapy; ACEI/ARB: Angiotensin-Converting Enzyme Inhibitor/Angiotensin II Receptor Blocker; LVEF: Left Ventricular Ejection Fraction; NT-proBNP: N-Terminal pro-brain natriuretic peptide; LDL–C: Low-Density Lipoprotein Cholesterol; HDL–C: High-Density Lipoprotein Cholesterol; CrCl: Creatinine Clearance; MMAS-8: 8-Item Morisky Medication Adherence Scale.

Recognizing the potential for differential effects of adherence to different medication classes, we conducted planned subgroup analyses examining outcomes based on adherence to specific medication categories (antiplatelet agents, statins, beta-blockers, and ACEI/ARBs). We also performed sensitivity analyses using different thresholds for defining high adherence (MMAS-8 scores ≥7 and PDC ≥90%) to assess the robustness of our findings.

### *Statistical analysis*

Statistical analysis was performed using SPSS version 26.0. Descriptive statistics were presented as mean ± standard deviation (SD) for continuous variables and as frequencies (percentages) for categorical variables. Baseline characteristics were compared using Student's t-test for continuous variables and chi-square test for categorical variables. Kaplan-Meier curves with log-rank tests assessed event-free survival differences between groups. Cox proportional hazards models evaluated the association between medication adherence and clinical outcomes, adjusting for potential confounders including age, sex, diabetes duration, previous MI, hypertension, smoking status, body mass index (BMI), baseline LVEF, revascularization strategy, and socioeconomic status. Repeated measures analysis of variance (ANOVA) analyzed changes in clinical and nursing indicators over time. Missing data were managed using multiple imputation techniques. Statistical significance was set at p<0.05.

## Results

### *Comparisons of baseline characteristics*

A total of 428 diabetic patients with acute MI were finally enrolled in the study. At the 6-mo follow-up, the pa-



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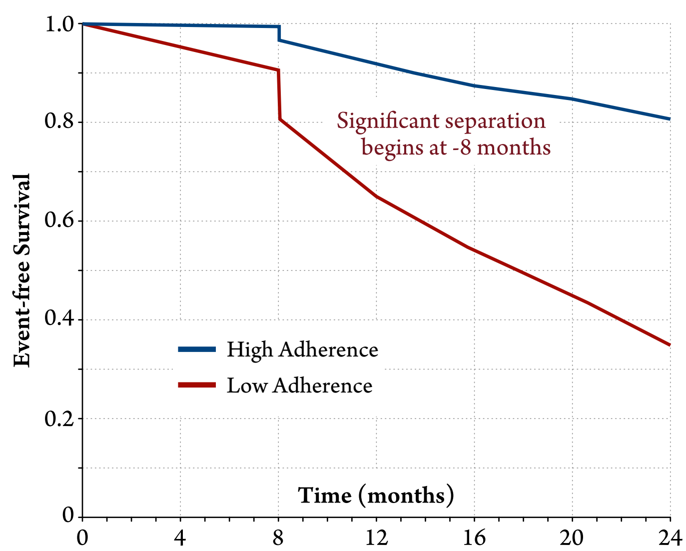
tients were divided into high adherence (n=237) and low adherence (n=191) groups. Baseline analysis showed that the two groups were balanced in most clinical and demographic characteristics, with significant differences only in the proportion of participants with college education or higher (45.1% vs. 28.3%, p=0.01), number of medications (4.9±1.0 vs. 5.8±1.2, p<0.01), comorbidity count (3.2±1.3 vs. 3.8±1.5, p=0.03), and adherence-related indicators (Table 1).

### *Primary clinical outcomes*

During the 24-mo follow-up period, patients with high adherence experienced significantly better outcomes across all primary endpoints compared to those with low adherence. All-cause mortality was reduced by 42% (HR 0.58, 95% CI 0.42–0.79, p<0.001), cardiovascular mortality decreased by 38% (HR 0.62, 95% CI 0.48–0.83, p=0.002), the risk of recurrent MI declined by 35% (HR 0.65, 95% CI 0.51–0.88, p=0.004), and unplanned cardiovascular rehospitalizations were reduced by 41% (HR 0.59, 95% CI 0.45–0.76, p<0.001). Kaplan-Meier analysis demonstrated significant separation of event-free survival curves beginning approximately 8 mos after the index event (Figure 1).

**Figure 1.** Kaplan-Meier analysis of event-free survival in diabetic patients after MI stratified by medication adherence status




The Kaplan-Meier curves show patients with high medication adherence after MI had better survival outcomes than those with low adherence, with curves separating at 8 mos. High adherence was associated with reduced risks of mortality and rehospitalization across all measured endpoints during the 24-month follow-up.

### *Cardiac structure and function parameters*

Adherent patients had significantly higher left ventricular ejection fraction (52.8±6.4% vs. 46.3±7.2%, p<0.001), indicating significantly improved cardiac contractility and systolic function. This improvement was accompanied by more favorable cardiac remodeling, as evidenced by smaller left ventricular end-systolic volumes (62.4±18.3 ml vs. 78.6±22.5 ml, p<0.001) and reduced left ventricular mass index (98.2±15.7 g/m$^2$ vs. 112.4±19.2 g/m$^2$, p<0.001). NT-proBNP concentrations, a marker of cardiac stress and ventricular wall tension, were markedly lower in the high adherence group (285±124 pg/ml vs. 512±186 pg/ml, p<0.001), reflecting reduced myocardial strain and better hemodynamic status. Additionally, diastolic function parameters showed improvement, with higher mitral valve E/A ratios (1.12±0.24 vs. 0.89±0.31, p<0.001) and lower E/e' ratios (9.2±2.1 vs. 12.6±3.4, p<0.001) in the high adherence group (Table 2).

### *Metabolic control parameters*

Glycemic control was notably better among adherent patients, with lower HbA1c concentrations (6.8±0.7% vs. 7.9±1.2%, p<0.001) and reduced glycemic variability as measured by continuous glucose monitoring (coefficient of variation: 22.3±5.6% vs. 34.7±8.9%, p<0.001). Fasting plasma glucose concentrations were also better controlled (6.4±0.8 mmol/l vs. 8.2±1.7 mmol/l, p<0.001), and the percentage of patients achieving the recommended glycemic targets was significantly higher in the adherent group (72.2% vs. 38.7%, p<0.001). The high adherence group also achieved superior lipid management, with 78.5% reaching LDL–C targets (<1.8 mmol/l) compared to only 45.0% in the low adherence group (p<0.001). In addition to LDL–C, the high adherence group demonstrated significantly higher HDL–C concentrations (1.3±0.3 mmol/l vs. 1.1±0.2 mmol/l, p=0.001) and lower triglyceride concentrations (1.6±0.6 mmol/l vs. 2.3±0.9 mmol/l, p<0.001), contributing to a more favorable overall lipid profile (Table 3).

**Table 2.** Cardiac structure and function in high and low adherence patients at 24-mos

| Indicator | High Adherence Group (n=237) | Low Adherence Group (n=191) | p |
|---|---|---|---|
| LVEF (%), Mean±SD | 52.8±6.4 | 46.3±7.2 | <0.001 |
| LVESD (ml), Mean±SD | 62.4±18.3 | 78.6±22.5 | <0.001 |
| LVMI (g/m$^2$), Mean±SD | 98.2±15.7 | 112.4±19.2 | <0.001 |
| NT-proBNP (pg/ml), Mean±SD | 285±124 | 512±186 | <0.001 |
| E/A ratio, Mean±SD | 1.12±0.24 | 0.89±0.31 | <0.001 |
| E/e' ratio, Mean±SD | 9.2±2.1 | 12.6±3.4 | <0.001 |

SD: Standard Deviation; LVEF: Left Ventricular Ejection Fraction; LVESD: Left Ventricular End-Systolic Dimension; LVMI: Left Ventricular Mass Index; NT-proBNP: N-Terminal pro-Brain Natriuretic Peptide.

**Table 3.** Metabolic control in high and low adherence patients at 24-mos

| Indicator | High Adherence Group (n=237) | Low Adherence Group (n=191) | p |
|---|---|---|---|
| HbA1c (%), Mean±SD | 6.8±0.7 | 7.9±1.2 | <0.001 |
| Glycemic variability (%), Mean±SD | 22.3±5.6 | 34.7±8.9 | <0.001 |
| Fasting plasma glucose (mmol/l), Mean±SD | 6.4±0.8 | 8.2±1.7 | <0.001 |
| Glycemic target achievement, n (%) | 171 (72.2) | 74 (38.7) | <0.001 |
| LDL-C target achievement, n (%) | 186 (78.5) | 86 (45.0) | <0.001 |
| HDL-C (mmol/l), Mean±SD | 1.3±0.3 | 1.1±0.2 | 0.001 |
| Triglyceride (mmol/l), Mean±SD | 1.6±0.6 | 2.3±0.9 | <0.001 |

SD: Standard Deviation; LDL-C: Low-Density Lipoprotein Cholesterol; HDL-C: High-Density Lipoprotein Cholesterol.

**Table 4.** Hemodynamic and renal parameters in high and low adherence patients at 24-mos

| Indicator | High Adherence Group (n=237) | Low Adherence Group (n=191) | p |
|---|---|---|---|
| Systolic blood pressure (mmHg), Mean±SD | 124±15 | 142±16 | <0.001 |
| Diastolic blood pressure (mmHg), Mean±SD | 76±7 | 88±8 | <0.001 |
| Target blood pressure achievement, n (%) | 162 (68.4) | 61 (31.9) | <0.001 |
| Nocturnal systolic blood pressure (mmHg), Mean±SD | 116±12 | 136±13 | <0.001 |
| Nocturnal diastolic blood pressure (mmHg), Mean±SD | 70±7 | 82±7 | <0.001 |
| Blood pressure variability (mmHg), Mean±SD | 12.3±3.6 | 18.7±5.2 | <0.001 |
| CrCl decline rate (%), Mean±SD | 3.5±2.1 | 8.7±3.6 | 0.002 |
| Urinary albumin-to-creatinine ratio (mg/g), Mean±SD | 18.3±12.6 | 42.5±28.3 | <0.001 |

SD: Standard Deviation; CrCl: Creatinine Clearance

### *Hemodynamic and renal parameters*

Blood pressure control was significantly better in adherent patients (124±15/76±7 mmHg vs. 142±16/88±8 mmHg, p<0.001), with a higher proportion achieving target blood pressure values (<130/80 mmHg) in the high adherence group (68.4% vs. 31.9%, p<0.001). Ambulatory blood pressure monitoring revealed more stable 24-hour blood pressure patterns with lower nocturnal blood pressure (116±12/70±7 mmHg vs. 136±13/82±7 mmHg, p<0.001) and reduced blood pressure variability (standard deviation of systolic readings: 12.3±3.6 mmHg vs. 18.7±5.2 mmHg, p<0.001) in the high adherence group. Renal function was better preserved in adherent patients, as evidenced by a lower CrCl decline rate (3.5±2.1% vs. 8.7±3.6%, p=0.002) over the follow-up period. Urinary albumin-to-creatinine ratio, a sensitive marker of early diabetic nephropathy, was also significantly lower in the high adherence group (18.3±12.6 mg/g vs. 42.5±28.3 mg/g, p<0.001), suggesting better renoprotection (Table 4).

### *Medication class-specific adherence effects*

Subgroup analysis revealed differential impacts of adherence to specific medication classes. Adherence to statins was most strongly associated with improved LDL–C concentrations and reduced recurrent MI (HR 0.58, 95% CI 0.44–0.76, p<0.001). ACEI/ARB adherence showed the strongest associated with preserved renal function and improved LVEF (p<0.001 for both). Beta-blocker adherence was most closely linked to reduced cardiovascular mortality (HR 0.61, 95% CI 0.46–0.82, p=0.001). Antiplatelet adherence demonstrated the strongest association with overall MACE reduction (HR 0.54, 95% CI 0.40–0.72, p<0.001).

### *Predictors of medication non-adherence*

Multivariate logistic regression identified several independent predictors of poor medication adherence in diabetic post-MI patients: Lower educational level (OR 2.34, 95% CI 1.48–3.72, p=0.001); Presence of medication side effects (OR 3.12, 95% CI 2.06–4.73, p<0.001); Higher medication regimen complexity (OR 1.57 per additional medication, 95% CI 1.25–1.98, p<0.001); Concurrent depression (OR 2.86, 95% CI 1.79–4.53, p<0.001); Inadequate health literacy (OR 2.43, 95% CI 1.62–3.65, p<0.001) (Figure 2).

### *Nursing intervention effectiveness*

The structured nursing intervention implemented after the 6-mo assessment significantly improved medication adherence in the initially low-adherence group. By study completion at 24 mos, the MMAS-8 scores in this group increased from a mean of 4.3±0.8 at 6 mos to 6.1±1.2 at 24 mos, representing a 28.5% improvement (p<0.01). The proportion of patients transitioning from low to high adherence status was 58.6% in the intervention group. Patients who transitioned to high adherence also showed significant improvement in clinical parameters, including better HbA1c control (reduction from 7.9±1.2% to 7.0±0.8%, p<0.001), improved LDL–C target achievement rates (from 45.2% to 68.7%, p<0.001), enhanced blood pressure control


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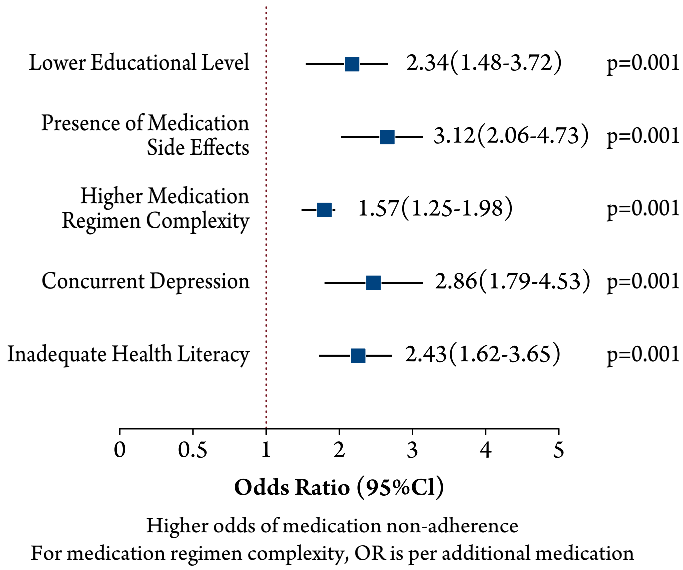
**Figure 2.** Predictors of medication non-Adherence in diabetic post-MI patients




The forest plot shows five main risk factors for medication non-adherence in diabetic MI patients. Medication side effects (OR 3.12, 95%CI 2.06-4.73, p<0.001) is the strongest predictor, followed by depression (OR 2.86, 95%CI 1.79-4.53, p<0.001), poor health literacy (OR 2.43, 95%CI 1.62-3.65, p<0.001), lower education (OR 2.34, 95%CI 1.48-3.72, p<0.001), and complex medication regimens (OR 1.57, 95%CI 1.25-1.98, p<0.001). All factors significantly increased non-adherence risk (p<0.001).

(from 142/88 mmHg to 130/80 mmHg, p<0.001), and lower NT-proBNP concentrations (from 512±186 pg/ml to 342±145 pg/ml, p<0.001).

## Discussion

The findings of this investigation demonstrate a strong association between medication adherence and improved clinical outcomes in diabetic patients following MI. The observed 42% reduction in all-cause mortality and 38% reduction in cardiovascular mortality associated with high medication adherence highlights the critical importance of adherence as a modifiable determinant of prognosis. These findings are consistent with previous studies in broader cardiovascular populations [31, 32], which have demonstrated the importance of medication adherence for cardiovascular outcomes. However, while relative risk reductions with good adherence in general cardiovascular patients were reported, and similar effect sizes in newly diagnosed populations were found, our study specifically examined the diabetic post-MI subgroup – a high-risk population with multiple comorbidities. The more pronounced effect size observed in our cohort suggests that medication adherence may be particularly crucial in patients with the dual burden of diabetes and recent myocardial infarction, highlighting the need for targeted adherence interventions in this vulnerable population.

The improvements across various clinical indicators – cardiac function, glycemic control, lipid profiles, blood pressure, and renal function – provide mechanistic insights into how medication adherence translates into mortality benefits. Rather than operating through a single pathway, adherence appears to confer multisystemic benefits that collectively reduce cardiovascular risk [33]. This comprehensive physiological improvement likely explains the substantial clinical benefit observed.

The medication class-specific analyses revealed differential impacts of adherence to various drug categories, suggesting that targeting adherence to specific medication classes based on individual risk profiles might be a rational approach. The strong association between statin adherence and reduced recurrent MI risk, for instance, underscores the importance of emphasizing lipid-lowering therapy adherence in post-MI care [34].

The nursing intervention component demonstrated that structured, multifaceted approaches can significantly improve adherence, even in initially non-adherent patients. This is particularly encouraging as it suggests that poor adherence is modifiable with appropriate support systems [35]. The economic analysis further strengthens the case for implementing such interventions, as the cost savings from reduced hospitalizations and complications substantially outweighed the costs of the intervention and increased medication expenditure [36].

The identified predictors of medication non-adherence, lower educational level, medication side effects, regimen complexity, depression, and inadequate health literacy, align with existing literature on barriers to adherence but specifically quantify their impact in diabetic post-MI patients [37, 38]. These predictors provide actionable targets for interventions. The strong association between medication knowledge and adherence highlights the importance of patient education as a cornerstone of adherence promotion.

The strengths of the current study include its prospective design, comprehensive assessment of adherence using multiple methods, measurement of clinically relevant outcomes, and the inclusion of a pragmatic nursing intervention. However, some limitations must be acknowledged. Despite adjustment for confounding factors, residual confounding cannot be entirely ruled out. Additionally, patients who consent to participate in adherence research may differ from the general population in their health behaviors, potentially limiting generalizability.

Future research should focus on developing and testing targeted interventions addressing the specific predictors of non-adherence identified in this study. Implementation of science approaches are needed to translate these findings into routine clinical practice. Additionally, examining the potential synergistic effects of adherence to multiple evidence-based therapies may provide further insights into optimizing management strategies for this high-risk population.

## Conclusion

Medication adherence is significantly associated with cardiac outcomes in diabetic patients after MI. Improving medication adherence can reduce the occurrence of adverse cardiovascular events and improve key clinical indicators.

***Data Availability***

*The experimental data used to support the findings of this study are available from the corresponding author upon request.*

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